HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARIES

For the

Diethylbenzene-Rich Streams Category

Prepared by:

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Ethylbenzene Panel HPV Task Group
Diethylbenzene Subteam

April 26, 2004

FREEZING POINT

Test Substance

Identity:	Diethylbenzene Blend
Purity:	92.3%
Remarks:	None

Method

Method:	ASTM D1015-89
GLP:	Yes
Year:	2003

Results

Value:	< -75°C
Remarks:	None

Conclusions Freezing point determined to be < -75°C

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions

References

Huntley, K. 2003. Determination of Freezing Point for a Diethylbenzene Blend. ABC Study No. 47932. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

BOILING POINT

Test Substance

Identity:	Diethylbenzene Blend
Purity:	92.3%
Remarks:	None

Method

Method:	Automated system, improved Siwoboloff method
GLP:	Yes
Year:	2003

Results

Value:	180.8 ± 1.7°C (454.0 K)
Remarks:	None

Conclusions Boiling Point is 180.8 °C

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions

References

Huntley, K. 2003. Determination of Boiling Point for a Diethylbenzene Blend. ABC Study No. 47933. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

VAPOR PRESSURE

Test Substance

Identity:	Diethylbenzene Blend
Purity:	92.3%
Remarks:	None

Method

Method:	Static
GLP:	Yes
Year:	2003

Results

Value:	210 ± 44 Pa at 10°C 310 ± 35 Pa at 20°C 530 ± 15 Pa at 30°C
Remarks:	None

Conclusions

Vapor pressure determined to be:
210 ± 44 Pa at 10°C
310 ± 35 Pa at 20°C
530 ± 15 Pa at 30°C

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions

References

Huntley, K. 2003. Determination of Vapor Pressure for a Diethylbenzene Blend. ABC Study No. 47934. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

WATER SOLUBILITY

Test Substance

Identity:	Diethylbenzene Blend
Purity:	92.3%
Remarks:	None

Method

Method:	Shake Flask
GLP:	Yes
Year:	2003

Results

Value:	15.7 + 1.4 μg/mL at 20°C
pH value:	7.54 (average of three samples)
Description of solubility:	Slightly soluble (0.1 to 100 mg/L)
Remarks:	None

Conclusions Water solubility is 15.7 μg/mL at 20°C

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions

References

Hahn J. A., K. 2003. Determination of Water Solubility for a Diethylbenzene Blend. ABC Study No. 47935. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

HYDROLYSIS (STABILITY IN WATER)

Test Substance

Identity:	Diethylbenzene-Rich Streams (CAS No.25340-17-4, 68608-82-2) Diethylbenzene-Rich Streams consist mainly of diethylbenzenes with small amounts of triethylbenzenes, butylbenzenes ,"other alkylbenzene," and ethylbenzene. All identified components are hydrocarbons.
Purity:	Not applicable

Method

Method/guideline followed:	Technical discussion
Type:	Not applicable
GLP:	Not applicable
Year:	Not applicable
Test Conditions	Not applicable

Results

Degradation % after time:	Not determined.
Results:	The hydrolysis rates of the components of the Diethylbenzene-Rich Streams category cannot be calculated because they contain no functional groups capable of hydrolysis.
Kinetics:	Not applicable
Breakdown products:	Not applicable
Conclusions	In the environment, hydrolysis will not contribute to the degradation of chemicals in the Diethylbenzene-Rich Streams category.

Data Quality

Reliability (Klimisch):	Not applicable
Remarks:	Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved. Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond. The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkylbenzenes, are not subject to hydrolysis

and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. The chemicals in this category are alkylbenzenes which contain only carbon and hydrogen and as such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Diethylbenzene-Rich Streams category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

References

Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA.

Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA.

Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.

HYDROLYSIS (STABILITY IN WATER)

Test Substance

Identity:	1,4-Diethylbenzene
Purity:	Not available

Method

Method/guideline followed:	OECD TG 111
Type:	Abiotic (hydrolysis)
GLP:	Yes
Year:	1993
Test Conditions	50 ± 0.1°C at each of pH 4.0, 7.0 and 9.0 for 5 days

Results.

Results:	Not hydrolysed at pH 4, 7 and 9
Kinetics:	Not applicable
Breakdown products:	Not applicable

Conclusions In the environment, hydrolysis will not contribute to the degradation of 1,4-diethylbenzene

Data Quality

Reliability (Klimisch):	2A
Remarks:	Guideline study without detailed documentation

References Unpublished Report (1993) (HPV/SIDS Test conducted by MITI, Japan. Test was performed in Chemicals Inspection and Testing Institute, Japan)

PHOTODEGRADATION (DIRECT)

Test Substance

Identity:	Diethylbenzene-Rich Streams (CAS No.25340-17-4, 68608-82-2) Diethylbenzene-Rich Streams consist mainly of diethylbenzenes with small amounts of triethylbenzenes, butylbenzenes ,"other alkylbenzene," and ethylbenzene. All identified components are hydrocarbons.
Purity:	Not applicable

Method

Method:	Technical Discussion
GLP:	Not applicable
Year:	Not applicable

Results

The components of the Diethylbenzene-Rich Streams category do not undergo photolysis with light at wavelengths >290 nm.

Conclusions

In the environment, direct photolysis will not significantly contribute to the degradation of chemicals in the Diethylbenzene-Rich Streams category.

Data Quality

Reliability (Klimisch): Not applicable

Remarks:

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment . Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule . Saturated hydrocarbons do not absorb light above 200 nm. Single ring aromatics also do not absorb sufficient light energy above 290 nm to cause photolysis.

The products in the Diethylbenzene-Rich Streams category consist almost entirely of single ring aromatics

that will not undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment.

References

Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA.

Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.

PHOTODEGRADATION (INDIRECT)

Test Substances

1,2 Diethyl Benzene (CAS 135-01-3)
1,3 Diethyl Benzene (CAS 141-93-5)
1,4 Diethyl Benzene (CAS 105-5-5)
Ethyl Benzene (CAS 100-41-4)

Method	Calculated rates of reaction with hydroxyl radicals and atmospheric half-lives using AOPWIN version 1.91, a subroutine of the computer program EPIWIN version 3.04 for diethylbenzenes and data from a monograph for ethylbenzene.
GLP	Not applicable
Year (study performed):	2004
Remarks:	The composition of Diethylbenzene-Rich Streams is mainly (>87.6%) diethylbenzenes with up to ~5% triethylbenzenes or up to 4.5% "other alkylbenzenes, and ~2% ethylbenzene possible. These compounds behave similarly so the major components and one with experimental data have been chosen as representative.
Test Conditions	Indirect photodegradation was equated with atmospheric oxidation potential with hydroxyl radical as the sole oxidant. Temperature: 25ºC Daytime OH Radical concentration: 1.5 x 10^6 radicals/cm^3
Results	Based on calculated values, products the Diethylbenzene-Rich Stream Category have an atmospheric half-life range of 9-18 hours as a result of indirect photolysis by hydroxyl radical attack. The residence times of components of the Diethylbenzene-Rich Stream Category in air are less than 1.5 days.
Conclusions	Atmospheric oxidation via hydroxyl radical can be a significant route of degradation for products in the Diethylbenzene-Rich Stream Category and limit the availability of the compounds in the environment**.**

Data Quality

Reliability (Klimisch)	2f Accepted calculation method
Remarks	The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life

range for products with the 4 CAS numbers listed under test substance.

AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

References

Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442.

Atkinson, R., Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds, J. Phys. Chem. Ref. Data Monograph No. 1 (1989).

Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299.

US EPA EPIWIN Suite AOPWIN version 1.91

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

Test Substance

Identity: 1,2-Diethyl Benzene [CAS 135-01-3]
Remarks: SMILES notation: CCc1ccccc1CC

Method

Test (test type): Calculated
Method: EQC Levels I, II, and III
Year (study performed): 2003
Remarks: Half-lives in water, soil and sediment estimated using EPIWIN. Chemical Assumptions: Molecular weight – 134.2; water solubility – 15.7 g/m^3; Vapor pressure – 310 Pa (20 °C); Log P_{ow} – 3.72; Melting point, -31.2 ^oC; half-life in air – 31.7 hours; half-life in water – 360 hours; half-life in soil – 360 hours; half-life in sediment – 1440 hours; all other parameters were default values. Level III model default emissions, continuous 1000 kg/hr releases to each compartment (air, water and soil).

Results

Fractions residing in air, soil, water and sediment were estimated**.**

	Level I	**Level II**	**Level III**
Air	99.0%	99.0%	1.14%
Water	0.18%	0.18%	51.4%
Soil	0.85%	0.85%	45.5%
Sediment	0.02%	0.02%	1.88%

Remarks: Since default assumptions for release estimates were used, resulting environmental concentrations are not provided.

Conclusions

These results indicated that 1,2-diethyl benzene will partition primarily to air under equilibrium conditions (Level I and II models), but to water and soil under the default equal loading of water, soil and air in the Level III model. Minimal material will reside in sediment.

Data Quality

Reliabilty (Klimisch): 2f
Remarks: Accepted calculation method

References

Trent University. 1999. Fugacity-based Environmental Equilibrium Partitioning Model. Version 2.2. Environmental Modeling Centre, Trent University, Peterborough, Ontario. (Available at http://www.trentu.ca/envmodel.)

US EPA EPIWIN Suite. (Estimates of half-lives in water, soil, sediment from QSAR).

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

Test Substance

Identity: 1,3-Diethylbenzene (CAS 141-93-5)
Remarks: SMILES notation: c(cccc1CC)(c1)CC

Method

Test (test type): Calculated
Method: EQC Levels I, II, and III
Year (study performed): 2003
Remarks: Half-lives in air, water, soil and sediment estimated using EPIWIN. Chemical Assumptions: Molecular weight – 134.22; water solubility – 15.7 g/m^3; Vapor pressure – 310 Pa (20 °C); Log P_{ow} – 4.44; Melting point, -83.9 ^oC; half-life in air – 18 hours; half-life in water – 360 hours; half-life in soil – 360 hours; half-life in sediment – 1440 hours; all other parameters were default values. Level III model default emissions, continuous 1000 kg/hr releases to each compartment (air, water and soil).

Results

Air, soil, water and sediment concentrations were estimated.

	Level I	Level II	Level III
Air	95.4%	95.4%	0.54%
Water	0.18%	0.18%	31.2%
Soil	4.3%	4.3%	61.7%
Sediment	0.10%	0.10%	6.6%

Remarks: Since default assumptions for release estimates were used, resulting environmental concentrations are not provided.

Conclusions

These results indicated that 1,3 diethylbenzene will partition primarily to air under equilibrium conditions (Level I and II models), but to soil and water under the assumed pattern of chemical release (equal loading of water, soil and air) in the Level III model. These results reflect the Level III model's loading pattern plus the estimated moderately long half-life in water and soil and short half-life in air.

Data Quality

Reliabilty (Klimisch): 2f
Remarks: Accepted calculation method

References

Trent University. 1999. Fugacity-based Environmental Equilibrium Partitioning Model. Version 2.2. Environmental Modeling Centre, Trent University, Peterborough, Ontario. (Available at http://ww.trentu.ca/envmodel

US EPA EPIWIN Suite. (Estimates of half-lives in water, soil, sediment from QSAR).

TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

Test Substance

Identity: 1,4-Diethyl benzene, (CAS 105-05-5)
Remarks: SMILES notation: CCc1ccc(CC)cc1

Method

Test (test type): Calculated
Method: EQC Levels I, II, and III
Year (study performed): 2003
Remarks: Half-lives in water, soil and sediment estimated using EPIWIN. Chemical Assumptions: Molecular weight – 134.22; water solubility – 15.7 g/m^3; Vapor pressure 310 Pa (20 °C); Log P_{ow} – 4.45; Melting point, -42.8 ^oC; half-life in air – 31.7 hours; half-life in water – 360 hours; half-life in soil – 360 hours; half-life in sediment – 1440 hours; all other parameters were default values. Level III model assumed continuous 1000 kg/hr releases to each compartment (air, water and soil).

Results

Air, soil, water and sediment concentrations were estimated.

	Level I	Level II	Level III
Air	95.3%	95.3%	0.56%
Water	0.18%	0.18%	31.0%
Soil	4.4%	4.4%	61.8%
Sediment	0.10%	0.10%	6.7%

Remarks: Since default assumptions for release estimates were used, resulting environmental concentrations are not provided.

Conclusions

These results indicated that 1,4-diethylbenzene will partition primarily to air under equilibrium conditions (Level I and II models), but to soil and water under the assumed pattern of chemical release (equal loading of water, soil and air) in the Level III model. These results reflect the Level III model's loading pattern plus the assumed moderately long half-life in water and soil and short half-life in air.

Data Quality

Reliabilty (Klimisch): 2f
Remarks: Accepted calculation method

References

Trent University. 1999. Fugacity-based Environmental Equilibrium Partitioning Model. Version 2.2. Environmental Modeling Centre, Trent University, Peterborough, Ontario. (Available at http://ww.trentu.ca/envmodel.)

US EPA EPIWIN Suite. (Estimates of half-lives in water, soil, sediment from QSAR).

BIODEGRADATION

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No.25340-17-4)
Purity:	Not specified

Method

Method/guideline followed:	EC Method C. 4-C, 1992
Type:	CO_2 evolution test (aerobic)
GLP:	Yes
Year:	1995
Contact time:	35 days
Inoculum:	Activated sludge
Remarks:	The test apparatus consisted of six glass 4-liter Erlenmeyer flasks containing two liters of modified biochemical oxygen demand (BOD) water. The test system was activated sludge collected from the Downingtown Regional Water Pollution Control Center (Pennsylvania) and screened through a 2 mm sieve and adjusted to a target solids level of 2500 mg/liter by diluting with settled sludge effluent. The adjusted sludge was aerated in semi-continuous activated sludge (SCAS) units until used in the preparation of the inoculum added to all flasks (up to 24 hours prior to study initiation). The sludge was not exposed to the test substance in the laboratory prior to addition to the test flasks. Test substance was added directly to the flasks to a final concentration of 10 mg/liter. The flasks were placed on a rotary platform shaker and mixed at 110 $\pm$ 10 rpm for the duration of the study. Incubation temperature was 22.2 to 23.2 ^{o}C.

Results

Degradation % after time:	4.7 after 28 days; 5.5 after 35 days
Results:	Mixed diethylbenzene stream is not readily biodegradable.
Kinetics:	Not determined
Breakdown products:	Not determined

Conclusions The biodegradation of mixed diethylbenzene under aerobic conditions has been adequately characterized.

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References	Marks, K. H., Crapo, K. C. and Doi, J. (1995). EC: CO_2 Evolution Test on Polyethylbenzene [Mixed Diethylbenzenes]. Unpublished Report by Roy F. Weston, Inc, Study No. 95-056. Conducted for Chevron Research and Technology Company.
Other Available Reports	MITI, Japan. 1993. Unpublished Report [1,4-Diethylbenzene]. Test was performed in Chemicals Inspection and Testing Institute. 4B: Not assignable; only secondary literature.

Other

Last changed:	September 4, 2001

BIODEGRADATION

Test Substance

Identity:	Aqueous extract of Gas Oil (British Petroleum Company) containing diethylbenzenes
Purity:	The concentration of total hydrocarbons was approx. 2 ppm in the solution to be assayed. Diethylbenzenes constituted about 2% of the hydrocarbons. In the analyses, 1,4-diethylbenzene was confounded with *n*-butylbenzene and 1,2-diethylbenzene with 1,3-dimethyl-5-ethylbenzene.

Method

Method/guideline followed:	n.a.
Type:	Disappearance (aerobic)
GLP:	No
Year:	1978
Contact time:	35 days
Inoculum:	Mixed autochthonous flora in clean ground water samples from Tuffenwies and Zurich, Switzerland, with a pH of 8.0, at 10 and 25 °C and microbial populations of 300-400 cells/ml
Remarks:	A Plexiglas column (4 cm wide, 114 cm long) was filled with quartz sand (grain size 0.4-0.63 mm) pretreated at 400°C for 12h. Homogeneous and reproducible packing in the filling operation was achieved by passing the sand through 3 sieves. The column porosity amounted to 40-41% and the water content at residual saturation was 12%. At a dosing rate of 60 ml h^{-1}, the detention time in the column (length = 87 cm) was approx. 2 h. At continuous percolation, the water content in the sand equilibrated at ~ 30% (v/v, residual air space ~ 10%). Samples of percolate were taken by suction through nylon membranes at underpressures smaller than the bubble pressure point. It was assured that all materials in contact with the aqueous hydrocarbon solution showed no adsorption or other reactions with the dissolved components. Each percolation experiment started with a newly prepared column. Prior to the infiltration of the hydrocarbon-polluted water, the system was flushed for 4 days with clean ground water. Concentration of total hydrocarbons was approx. 2 ppm in the solution to be assayed. Samples were taken at two depths (20 cm and 90 cm below the point of infiltration) and analyzed by gas chromatography. Two flow rates (60 ml h^{-1} in experiment A and 120 ml h^{-1} in experiment B) were studied.

Results

Degradation % after time:	Only after a considerable lag phase of three to four days, individual hydrocarbon concentrations started to decrease at a measurable rate. Once the cell count exceeds 10^4-10^5 cells $m1^{-1}$, degradation of hydrocarbons in the aqueous phase progresses very rapidly. No significant concentration gradient of total hydrocarbons between the two sampling depths was observed. After 8 and 10 days of continuous percolation at rates of 60 ml h^{-1} and 120 ml h^{-1} respectively, a steady state of zero hydrocarbons, detectable with gas chromatography, developed at the percolation depth of 20 cm and (somewhat earlier) at 90 cm. During this period, however, intermediate degradation products accumulate in the water phase. It takes an additional 5 days for the build up of populations of bacterial species capable of eliminating these secondary products. In total, roughly 14 days (at 10°C) were required from the start of contamination for establishing a steady state of complete oxidative elimination of the hydrocarbons.
Kinetics:	Not determined
Breakdown products:	Not determined
Conclusions	Some species of the ubiquitous microflora in ground water are capable of using the water-soluble fraction of gas oil as the only carbon source under suitable conditions (i.e. unlimited supply of oxygen and nitrogen). Diethylbenzenes are cooxidized. A long lag phase (about 4 days) preceding degradation is indicative of a small initial number of bacteria capable of oxidizing hydrocarbons. The low experimental temperature of 10°C contributed of course to the slow start of bacterial development (in an experiment carried out at 25°C, the lag phase reduced to 1 day). In nature, the extent of hydrocarbon degradation might be limited by the available amount of oxygen and possibly nitrogen sources.

Data Quality

Reliability (Klimisch):	3b; significant methodological deficiencies
Remarks:	1,2- and 1,4-diethylbenzene both coeluted with other hydrocarbons. The diethylbenzenes were cooxidized with a much larger amount of other hydrocarbons.

Reference	Kappeler, Th., and Wuhrmann, K. (1978). Microbial Degradation of the Water-Soluble Fraction of Gas Oil – I, *Water Research*, 12 , 327- 334.

Other

Last changed:	April 16, 2004

BIODEGRADATION

Test Substance

Identity:	Aqueous extract of Gas Oil (British Petroleum Company) containing diethylbenzenes. An aqueous solution of hydrocarbons was prepared by shaking1 ml of gas oil with 1 1iter of ground water for l0 min. After centrifugation of the emulsion (4700 g), the oil phase was separated from the water and sterilized by membrane filtration (Sartorius SM 116 regenerated cellulose, pore size 0.2 μm).
Purity:	The total concentration of hydrocarbons was approx. 2 ppm in the solution to be assayed. Diethylbenzenes constituted about 2% of the hydrocarbons. In the analyses by extraction with CH_2Cl_2 and GC/MS, 1,4-diethylbenzene was confounded with *n*-butylbenzene and 1,2-diethylbenzene with 1,3-dimethyl-5-ethylbenzene.

Method

Method/guideline followed:	n.a.
Type:	Disappearance (aerobic)
GLP:	No
Year:	1978
Contact time:	35 days
Inoculum:	1. Mixed autochthonous flora in clean ground water samples from Tuffenwies and Zurich, Switzerland, with a pH of 8.0, at 10 and 25 deg C and microbial populations of 300-400 cells/ml. 2. A large number of bacterial strains were isolated in the course of percolation experiments (Kappeler, Th., and Wuhrmann, K., 1978) by plating the percolate on nutrient broth agar. Four isolates (A, B, C, D) of the genus Pseudomonas were used in the degradation experiments. Strains were maintained on agar slants and precultured in nutrient broth.
Remarks:	2 1 of aqueous hydrocarbon solution in 2.8-l sealed flasks were incubated at 10°C. In assays with the natural microbial flora of ground water, the aqueous solution was incubated directly. In tests with pure strains, the solution was sterilized as indicated, prior to inoculation.. A control run where bacterial activity was stopped by $HgC1_2$ showed no alteration of the hydrocarbon solution within 35 days.

Results

Degradation % after time:

A measurable concentration decrease of hydrocarbons started after a lag phase of 5-6 days. Individual components were degraded at different rates. For example. 1, 2, 4-trimethylbenzene, originally present at the highest concentration, was eliminated within two days after the beginning of visible degradation. 1, 2, 3-trimethylbenzene and 1,3,5-trimethylbenzene, however, are fairly resistant and disappear only after 11-12 days. Similarly, m- and p-xylene are degraded much faster than o-xylene. In experiments with initial hydrocarbon concentrations exceeding 2.0 to 2.1 mg 1^{-1} degradation ceased after 10 days. Addition of NH_4C1 resulted in further breakdown.

Degradation of hydrocarbons is combined with massive bacterial growth in ground water. The cell count after inoculation was about 130 ml^{-1}. Exponential growth started after a short lag phase of about 1 day; at a detectable hydrocarbon decrease, the cell concentrations amounted already to 10^4-10^6 ml^{-1}. Maximum cell densities of $2 \cdot 10^6$- $4 \cdot 10^6$ ml^{-1} were reached at exhaustion of the substrate. The cell counts suggest a statistical "generation time" of the microbial flora of roughly 10 h (10°C). The initial pH of 7.9 decreased to 7.3 within 14 days.

Kinetics:

In the microbial degradation at 10ºC of the water-soluble fraction of gas oil exposed to the autochthonous microflora in ground water the 1,3-diethylbenzene concentration (nl l^{-1}) started at 6.6 and was 6.1, 5.6, 4.9, 2.9 and 0 at 5,6,7,8 and 9 days respectively. The 1,4-diethylbenzene/*n*-butylbenzene concentration was 8.9 nl l^{-1} initially and was 5.3, 4.5, 3.3, and 0 nl l^{-1} at 5,6,7, and 8 days respectively. The 1,2-diethylbenzene/1,3-dimethyl-5-ethylbenzene concentration was 19.3 nl l^{-1} initially and was 17.5, 17.4, 16.4, 13.8, 9.9, 5.7, 2.6 and 0 nl l^{-1} at 5, 6, 7, 8, 9, 10, 11 and 12 days respectively.

Breakdown products:

2-ethylstyrene and 1-(2-ethylphenyl)ethanol from 1,2-diethylbenzene with strain D.

Conclusions

Some species of the ubiquitous microflora in ground water are capable of using the water-soluble fraction of gas oil as the only carbon source under suitable conditions (i.e. unlimited supply of oxygen and nitrogen). Diethylbenzenes are cooxidized.

Two degradation pathways for aromatic compounds are operative, i.e. 1) the oxidation of the alkyl substituents followed by ring opening and 2) direct oxidation of substituted or unsubstituted mono or polynuclear aromatic.

The first step in the degradation of the aromatics by strain B and D seems to be similar. The metabolism of the ethylated derivatives proceeds via dehydrogenation of the alkylated side chain, followed by a hydroxylation.

Ortho-substituted benzenes are relatively resistant to biodegradation.

Data Quality

Reliability (Klimisch): 3b; significant methodological deficiencies

Remarks: 1,2- and 1,4-diethylbenzene both coeluted with other hydrocarbons. The diethylbenzenes were cooxidized with a much larger amount of other hydrocarbons.

References

Kappeler, Th., and Wuhrmann, K. (1978a). Microbial Degradation of the Water-Soluble Fraction of Gas Oil – I, *Water Research*, 12 , 327- 334.

Kappeler, Th., and Wuhrmann, K. (1978). Microbial Degradation of the Water-Soluble Fraction of Gas Oil – II Bioassays with Pure Strains, *Water Research*, 12 , 335- 342.

Other

Last changed: April 16, 2004

BIODEGRADATION

Test Substance

Identity:	Water-soluble fraction of gas oil. 1,3-Diethylbenzene was about 0.2% of the hydrocarbons when 10 L of water was contacted with 100 mL of gas oil. 1,4-Diethylbenzene was only observed in a sample of 10 L of water contacted with 500 mL of gas oil, whose composition was not quantified. 1,2-diethylbenzene was not observed.
Purity:	Not specified. 90% of the components were identified by gas chromatography based on retention times (Kovat's indices).

Method

Method/guideline followed:	n.a,
Type:	Disappearance (aerobic)
GLP:	No
Year:	1978
Contact time:	10-14 days
Inoculum:	North Sea coast water
Remarks:	In the first experiment (A) 10 liters of phosphorus- and nitrogen-free artificial sea water was contacted with 100 mL of gas oil at 20 °C for three days while being stirred very slowly. The water layer was sampled in four portions. Sample I was analyzed for dissolved hydrocarbons by extraction with pentane, purification of the extract and high-resolution gas chromatography. Samples II and III were supplemented with nitrogen and phosphorus salts and inoculated with 5 ml North Sea coast water and incubated at 25 °C for 10 days. Sample III had 50 mg/liter copper sulfate added to inhibit microbial activity. In the second experiment (B) 10 liters of fresh water was contacted with 500 ml of gas oil, and samples were taken to study the biodegradation after 2, 4, 7 and 14 days incubation at 20 °C. Qualitative assessment of gas chromatograms was used to assess the rate of removal of separate species (but only the initial and 14-day chromatograms were shown).

Results

Degradation % after time:	The oxidation rates of 1,3-and 1,4-diethylbenzene were "moderate,."
Kinetics:	Not determined
Breakdown products:	Not determined

Conclusions	Some species of the ubiquitous microflora in North Sea coast water are capable of using the water-soluble fraction of gas oil as the only carbon source under suitable conditions (i.e. unlimited supply of oxygen and nitrogen). 1,3- and 1,4-diethylbenzenes were among the species cooxidized. No conclusion can be drawn about 1,2-diethylbenzene. The citation in HSDB erroneously reported that 1,2-diethylbenzene was observed to biodegrade.
Data Quality	
Reliability (Klimisch):	3b; significant methodological deficiencies
Remarks:	Inadequate identification of diethylbenzenes. Cooxidation, rather than biodegradation of diethylbenzenes alone, affects the assessment of acclimatization. The concentration of microorganisms was unknown. The concentrations of 1,4-diethylbenzene, when it could be observed, is not given. There was a general lack of quantitation.
Reference	Van der Linden, A. C.,1978. Degradation of Oil in the Marine Environment, Chapter 6 in *Dev. Biodegrad. Hydrocarbons,* 1, 165-200, ed.. R. J. Watkinson, Applied Science Publishers, London
Other	
Last changed:	April 18, 2004

BIODEGRADATION

Test Substance

Identity:	1,2 Diethyl Benzene (CAS 135-01-3) 1,3 Diethyl Benzene (CAS 141-93-5) 1,4 Diethyl Benzene (CAS 105-5-5)
Purity:	n.a.
Remarks:	The composition of Diethylbenzene-Rich Streams is mainly (>87.6%) diethylbenzenes with up to ~5% triethylbenzenes or up to 4.5% "other alkylbenzenes," and ~2% ethylbenzene possible. These compounds behave similarly so the major components have been chosen as representative.

Method

Method/guideline followed:	Calculated inherent biodegradation with BIOWIN version 4.01, a subroutine of the computer program EPIWIN version 3.04 for diethylbenzenes.
Type:	QSAR
GLP:	n.a.
Year:	2004
Contact time:	n.a.
Inoculum:	n.a.

Results

Degradation % after time:	Primary biodegradation is defined by disappearance of the compound. Ultimate biodegradation is mineralization (oxidation of intermediates to CO_2). The prediction for all isomers on the rating scale of 4.0 = days; 3.5 = days to weeks, 3.0 = weeks and 2.5 = weeks to months is 3.52 (days-weeks) for primary biodegradation and 2.75 (weeks-months) for ultimate biodegradation. For use with the EQC Level III model of environmental fate, EPIWIN converts the BIOWIN ultimate biodegradation estimate to a scale of default values that gives all diethylbenzenes a half-life in water of 360 hours; a half-life in soil of 360 hours; and a half-life in sediment of 1440 hours.
Kinetics:	n.a.
Breakdown products:	n.a.
Remarks	This algorithm does not capture the generalization that *o*-substituted alkyaromatic compounds degrade slower than the *m*- and *p*-isomers.

Conclusions	The diethylbenzenes are inherently biodegradable under aerobic conditions**.**
Data Quality	
Reliability (Klimisch):	2f , accepted calculation method
Remarks:	This estimation method is employed within the EQC Level III model of environmental fate.
References	US EPA EPIWIN Suite, BIOWIN version 4.01
	Meylan, W. and Howard, P., 2000. User's Guide for BIOWIN, Biodegradation Probability Program v4.0 for Microsoft Windows, Syracuse Research Corporation, North Syracuse, NY.
Other	
Last changed:	April 16, 2004

BIOACCUMULATION

Test Substance

Identity:	1,4-Diethylbenzene
Purity:	> 95 %

Method

Method/guideline followed:	OECD TG 305C
Type:	measured; flow-through
GLP:	Yes
Year:	1992
Species:	Carp
Exposure period:	6 weeks
Temperature:	25 °C
Concentration:	(1) 20 µg/l (2) 2 µg/l
Remarks:	None

Results

BCF:	(1) 362 - 598 (2) 320 - 629

Conclusions Moderate potential of 1,4-diethylbenzene to bioconcentrate

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction

Reference MITI, Japan (1992) Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan, Edit CITI, Japan (1992).

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Other

Last changed:	April 21, 2004

ACUTE TOXICITY TO FISH

Test Substance:	Diethylbenzene Blend
Purity:	92.3% as diethylbenzenes
Remarks:	Blend prepared from equal volumes of diethylbenzene samples provided by Sterling Chemicals, Inc., BP Amoco Chemical Company, and Dow Chemical Company. Purity and identity were determined in ABC Laboratories Study No. 47928.
Method:	Fish Acute Toxicity Test
Guideline:	OECD 203. Other: OECD Guidance document on Aquatic Toxicity of Difficult Substances and Mixtures, 2000
Test type:	Acute, 96 hour
GLP:	Yes
Year:	2003
Analytical Procedures:	HP 5890 Series II GC equipped with a flame ionization detector used to analyze "new" solutions at 0 and 72 hours and "old" solutions at 24 and 96 hours. Minimum Quantifiable Limit (MQL): 0.0790 mg a.i./L
Species, strain:	*Oncorhynchus mykiss* (Rainbow Trout)
Test details:	Static: four replicates with 3 individuals per replicate. Test chambers were 3.5 L glass jars sealed with glass plates and with zero headspace, containing 3.9 L. Fish were approximately 3 months old, with total length 40 to 53 mm and wet weight of 0.488 to 1.247 g. Loading rate was 0.665 g of fish per liter.
Statistical methods:	LC_{50} and 95% confidence limits calculated by Probit method or Trimmed Spearman-Karber method
Remarks:	Individual test solutions were prepared by adding an appropriate volume of a working standard or primary standard to 18 L of dilution water resulting in nominal concentrations of 0.50, 1.0, 2.0, 4.0 and 8.0 mg a.i./L. Working standards were prepared in acetone. The vehicle control contained an acetone concentration of 0.10 mL/L. Each 18-L volume of the controls and test substance treatments was covered with a glass plate and stirred with a Teflon stir bar for approximately one hour. The stirring was adjusted to provide a vortex <10% of the solution depth. After stirring, the phases were allowed to separate for approximately 30 minutes. Beginning with the control and continuing up to the highest treatment, the bottom aqueous phase was drawn from approximately one inch above the bottom of each glass jar using a glass siphon tube into the test chambers. Fresh test solutions were prepared daily.

Results

Nominal concentrations (mg a.i./L): 0 (control), 0 (vehicle control; 0.10 mL acetone/L), 0.50, 1.0, 2.0, 4.0, and 8.0

Measured concentrations (mg a.i./L): <0.0790 (control), <0.0790 (vehicle control), 0.308, 0.675, 1.17, 1.64, and 2.47 mg a.i./L

Duration: 96 hours

Endpoint: LC50 = 0.673 mg a.i./L

Statistical range: (95% confidence interval: 0.474 to 0.869 mg a.i./L)

Remarks:

Mortality at	24hr	48hr	72hr	96hr	(% at 96hr
Control	0/12	0/12	0/12	0/12	0%
Vehicle control	0/12	0/12	0/12	0/12	0%
0.308 mg a.i./L	0/12	0/12	1/12	1/12	8%
0.675 mg a.i./L	3/12	6/12	7/12	7/12	58%
1.17 mg a.i./L	1/12	1/12	2/12	9/12	75%
1.64 mg a.i./L	11/12	11/12	11/12	11/12	92%
2.47 mg a.i./L	8/12	9/12	12/12	12/12	100%

Remarks: All results were based upon mean measured concentrations.

Data quality

Reliability (Klimish): 1A

Remarks: Reliable without restriction

Quality check

QA review within organization doing study
Report or publication reviewed by technically qualified person not associated with organization doing study

References

Hicks, S. L. 2003. Acute Toxicity of a Diethylbenzene Blend to the Rainbow Trout, *Oncorhynchus mykiss*, determined under Static-renewal Test Conditions. ABC Laboratories, Inc., Columbia, Missouri (USA). ABC Study No. 47929. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

Other
Remarks:

Prepared by: Stephen L. Hicks (ABC Laboratories, Inc.)
Date: 13 August 2003
Revised: M. C. Harrass (BP Amoco Chemicals)
Date: 19 August 2003

ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance:	Diethylbenzene Blend
Purity:	92.3% as diethylbenzenes
Remarks:	Blend prepared from equal volumes of diethylbenzene samples provided by Sterling Chemicals, Inc., BP Amoco Chemical Company, and Dow Chemical Company. Purity and identity were determined in ABC Laboratories Study No. 47928.
Method:	Daphnia sp., Acute Immobilization Test Guideline: OECD 202 Other: OECD Guidance document on Aquatic Toxicity of Difficult Substances and Mixtures, 2000
Test type:	Acute, 48 hour
GLP:	Yes
Year:	2003
Analytical Procedures:	HP 5890 Series II GC equipped with a flame ionization detector used to analyze "new" solutions at 0 and 24 hours and "old" solutions at 24 and 48 hours. Minimum Quantifiable Limit (MQL): 0.0790 mg a.i./L
Species, strain:	Daphnia magna, <24 hours old
Test details:	Static renewal: four replicates with 5 individuals per replicate. Test chambers were eight-ounce glass jars completely filled with test solution and sealed with a glass plate, containing 275 mL.
Statistical methods:	EC_{50} and 95% confidence limits calculated by Probit method or Trimmed Spearman-Karber method
Remarks:	Individual test solutions were prepared by adding an appropriate volume of a working standard or primary standard to 3.0 L of dilution water resulting in nominal concentrations of 0.50, 1.0, 2.0, 4.0 and 8.0 mg a.i./L. Working standards were prepared in acetone. The vehicle control contained an acetone concentration of 0.10 mL/L. Each 3.0-L volume of the controls and test substance treatments was covered with a glass plate stirred with a Teflon stir bar for approximately one hour. The stirring was adjusted to provide a vortex <10% of the solution depth. After stirring, the phases were allowed to separate for approximately 30 minutes. Beginning with the control and continuing up to the highest treatment, the bottom aqueous phase was drawn from approximately one inch above the bottom of each glass jar using a glass siphon tube into the test chambers. Fresh test solutions were prepared daily.

Results

Nominal concentrations (mg a.i./L): 0 (control), 0 (vehicle control; 0.10 mL acetone/L), 0.50, 1.0, 2.0, 4.0, and 8.0

Measured concentrations (mg a.i./L): <0.0790 (control), <0.0790 (vehicle control), 0.374, 0.665, 1.07, 1.97, and 2.70 mg a.i./L

Duration: 48 hours

Endpoint: EC50 = 2.01mg a.i./L

Statistical range: (95% confidence interval: 1.72 to 2.28 mg a.i./L)

Remarks:

Mortality at:	24hr	48hr	% at 48 hr
Control	1/20	1/20	5%
Vehicle Control	0/20	0/20	0%
0.374 mg a.i./L	0/20	0/20	0%
0.665 mg a.i./L	0/20	0/20	0%
1.07 mg a.i./L	0/20	0/20	0%
1.97 mg a.i./L	3/20	11/20	55%
2.70 mg a.i./L	2/20	16/20	80%

Temperature of the test solutions ranged from 19.4 to 20.2°C, dissolved oxygen concentration ranged from 7.6 to 9.4 mg/L, and pH ranged from 8.25 to 8.36.

Remarks: All results were based upon mean measured concentrations.

Data Quality

Reliability (Klimish): 1A

Remarks: Reliable without restriction

Quality Check

QA review within organization doing study
Report or publication reviewed by technically qualified person not associated with organization doing study

References

Hicks, S. L. 2003. Acute Toxicity of a Diethylbenzene Blend to the Water Flea, *Daphnia magna*, determined under Static-renewal Test Conditions. ABC Laboratories, Inc., Columbia, Missouri (USA). ABC Study No. 47930. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

Other

Remarks: Prepared by: Stephen L. Hicks (ABC Laboratories, Inc.)
Date: 13 August 2003
Revised: M. C. Harrass (BP Amoco Chemicals)
Date: 19 August 2003

ACUTE TOXICITY TO AQUATIC ALGAE OR PLANTS

Test Substance:	Diethylbenzene Blend
Purity:	92.3% as diethylbenzenes
Remarks:	Blend prepared from equal volumes of diethylbenzene samples provided by Sterling Chemicals, Inc., BP Amoco Chemical Company, and Dow Chemical Company. Purity and identity were determined in ABC Laboratories Study No. 47928.
Method:	Algal Inhibition Test
Guideline:	OECD 201 Other: OECD Guidance document on Aquatic Toxicity of Difficult Substances and Mixtures, 2000
GLP:	Yes
Year:	2003
Analytical Procedures:	HP 5890 Series II GC equipped with a flame ionization detector used to analyze solutions at 0, 24, 48, and 72 hours. Minimum Quantifiable Limit (MQL): 0.0702 mg a.i./L
Species, strain:	*Pseudokirchneriella subcapitata* (Formally known as *Selenastrum capricornutum*)
Test details:	Static: nine replicates prepared at test initiation of which 3 replicates were sacrificed at each observation time point (24, 48, and 72 hours). Initial algal cell concentrations were approximately 10000 cells/mL. Test chambers were 125-mL Erlenmeyer flasks completely filled with test solution and sealed with a glass stopper. The volume in each flask was 145 mL. Flasks were incubated at 24 ±2°C and with continuous oscillation of 100 rpm, under continuous illumination of 8,600 ± 10% lux, provided by cool-white fluorescent lamps.
Statistical methods:	The control groups (control and vehicle control) were evaluated to determine whether or not they could be pooled by comparing the 72-hour means for the growth parameters of area under the growth curve and growth rate. Tests for normality and homogeneity of variance were performed on the control data and then the planned comparison, or Least Significant Difference (LSD) test, was performed by inspecting the p value for the t-test between control means. An analysis of variance (ANOVA) using SAS and a one-way Dunnett's comparison to the vehicle control for area under the growth curve data and pooled controls for growth rate data was conducted to determine the no-observed effect concentrations (NOEC). The EC_{50} values and their 95% confidence limits were calculated using nonlinear (weighted) regression. The nonlinear modeling procedure developed a logistic (sigmoid-shaped) model which was fit to the data with percent inhibition as the

dependent variable and concentration as the independent variable. The percent inhibition was calculated compared to the vehicle control for the area under the growth curve data, and to the pooled controls for the growth rate data.

Remarks: Individual test solutions were prepared by adding an appropriate volume of a working standard or primary standard to 2.0 L of freshwater algae media resulting in nominal concentrations of 0.50, 1.0, 2.0, 4.0 and 8.0 mg a.i./L. Working standards were prepared in acetone. The vehicle control contained an acetone concentration of 0.10 mL/L. Each 2.0-L volume of the controls and test substance treatments was covered with a glass plate stirred and with a Teflon stir bar for approximately one hour. The stirring was adjusted to provide a vortex <10% of the solution depth. After stirring, the phases were allowed to separate for approximately 30 minutes. Beginning with the control and continuing up to the highest treatment, the bottom aqueous phase was drawn from the bottom of each bottle through the outlet into the test flasks. Flasks were not re-sampled because the test design called for zero headspace.

Results

Nominal concentrations (mg a.i./L): 0 (control), 0 (vehicle control; 0.10 mL acetone/L), 0.50, 1.0, 2.0, 4.0, and 8.0

Measured concentrations (mg a.i./L): <0.0702 (control), <0.0702 (vehicle control), 0.292, 0.547, 1.14, 2.27, and 3.35 mg a.i./L

Duration: 72 hours

Endpoint -Growth: EC50 = 1.21 mg a.i./L

Endpoint -Biomass: EC50 = 1.00 mg a.i./L

Statistical range - Growth: 95% confidence interval: 0.650 to 1.78 mg a.i./L

Statistical range - Biomass: 95% confidence interval: 0 to 2.81 mg a.i./L

Remarks:

Cell Density (x10000 cells/mL) at:	24h	48hr	72hr
Control	2.0	15	61
Vehicle Control	1.9	12	72
0.292 mg a.i./L	2.5	12	68
0.547 mg a.i./L	2.2	13	63
1.14 mg a.i./L	1.2	2.2	16
2.27 mg a.i./L	0.92	0.82	0.81
3.35	1.0	0.71	0.77

Biomass (calculated as area under the growth curve) was statistically different for control and vehicle (solvent) control; treatments were thus compared against vehicle control for biomass. Growth rate was not statistically

different for control and vehicle control; treatments were compared against pooled control values for growth. Biomass and growth rates of the 3 highest concentrations were statistically reduced at all three observation times. The 72-hr NOEC for both biomass and growth was 0.547 mg a.i./L

The temperature of the solutions ranged from 23.6 to 24.8°C and the pH ranged from 7.75 to 9.63. Increased pH values were associated with algal growth.

Conclusions: 72 hours growth EC50 = 1.21 mg a.i./L (95% confidence interval: 0.650 to 1.78 mg a.i./L) and biomass EC50 = 1.00 mg a.i./L (95% confidence interval: 0 to 2.81 mg a.i./L) for a representative freshwater unicellular green alga.

Remarks: All results were based upon mean measured concentrations.

Data Quality

Reliability (Klimish): 1A

Remarks: Reliable without restriction

Quality Check

QA review within organization doing study
Report or publication reviewed by technically qualified person not associated with organization doing study

References

Hicks, S. 2003. Toxicity of a Diethylbenzene Blend to the Unicellular Green Alga, *Selenastrum capricornutum*. ABC Laboratories, Inc., Columbia, Missouri (USA). ABC Study No. 47931. Sponsored by American Chemistry Council Ethylbenzene Panel.

ABC Laboratories, Inc. 2003. Determination of Purity and Identity for a Diethylbenzene Blend. ABC Study No. 47928. Sponsored by American Chemistry Council Ethylbenzene Panel.

Other

Remarks: Prepared by: Stephen L. Hicks (ABC Laboratories, Inc.)
Date: 13 August 2003
Revised: M. C. Harrass (BP Amoco Chemicals)
Date: 19 August 2003

ANALYTICAL METHOD VALIDATION

Test Substance:

Identity	Diethylbenzene Blend
Purity	92.3%

Method

Test type	Analytical Monitoring: HP 5890 Series II GC equipped with a flame ionization detector.
GLP Compliance:	Test performed in compliance with U.S. Environmental Protection Agency Toxic Substances Control Principles of Good Laboratory Practice
Statistical Methods:	Calculation of mean and standard deviation; calculation of standard curve by linear regression using least-squares method
Test Conditions:	Triplicate 50 mL samples of freshwater and freshwater algal media were prepared by spiking 50 mL volumes of control water in culture tubes with diethylbenzene blend. The samples were fortified at concentrations which bracketed the expected nominal concentrations of the definitive toxicity studies. Fortification levels were 0.00 (control), 0.107, and 18.8 mg/L for both water types. Each sample was partitioned three times with 5 mL toluene aliquots. Extracts were collected in separate culture tubes. The combined toluene extracts were evaporated under a gentle stream of nitrogen gas to appropriate volumes.
Results:	Recoveries for freshwater method validation samples at concentrations of 0.107 and 18.8 mg/L ranged from 95 to 118%, with an average recovery of 104 ∀ 9.2%. Recoveries for freshwater algal media method validation samples at concentrations of 0.107 and 18.8 mg/L ranged from 93 to 111%, with an average recovery of 101 ∀ 7.0%. The MQL, MDL and PQL were determined to be 0.0632 mg/L, 0.590 mg/L and 2.95 mg/L, respectively.

References:

Leek, Tom. 2003. Validation of analytical methods for use in the determination of a Diethylbenzene blend in various media used in environmental toxicity studies. ABC Study No. 47927. Sponsored by American Chemistry Council Ethylbenzene Panel.

Additional References:

U.S. Environmental Protection Agency. 1989. Toxic Substances Control; Good Laboratory Practice Standards; Final Rule (40 CFR, Part 792). *Federal Register*, 54(158): 34043-34050.

American Society for Testing and Materials (ASTM). 1997. Standard Guide for Conducting Static 96-hour Toxicity Tests with Microalgae. ASTM Designation E1218-97a.

American Public Health Association, American Water Works Association, Water Environmental Federation. 1992. *Standard Methods for the Examination of Water and Wastewater*. 1030 E: 1-11.

U.S. Environmental Protection Agency. July 1, 1990. Final Rule. Definition and Procedure for the Determination of the Method Detection Limit - Revision 1.11. *Federal Register*, 40 CFR, Part 136, Appendix B. pp 537-539.

Other

Source

Performing Laboratory: ABC Laboratories, Inc.
7200 E. ABC Lane
Columbia, Missouri 65202
Study Number: 47927

ACUTE ORAL TOXICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated

Method

Method/guideline followed:	FIFRA/TSCA guidelines
Type:	LD_{50}
GLP:	Not stated
Year:	1987
Species/Strain:	Sprague-Dawley rats
Sex:	male and female
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Oral/gastric intubation
Remarks:	At the start of experiment, animals were about 9 to 12 weeks of age with a weight of 292 to 355 grams for males, and 224 to 253 grams for females. Room temperature was 67 to 76°F, and relative humidity was between 30 to 70% during the study. Animals were observed for 14 days postdose.

Results

LD_{50} value:	= 2050 mg/kg (confidence range 1770 to 2330 mg/kg) Number of deaths: 1700 mg/kg = 1 dead on day 3 (1 male); 1 dead at day 6 (1 female) 2500 mg/kg = 91 dead at 23 hours (1 female); 6 dead on day 2 (5 males and 1 female); 2 dead day 3 (2 females) 3500 mg/kg = 1 dead at 23 hours (1 female); 1 dead at day 1 (1 male); 6 dead at day 2 (3 males and 3 females); 1 dead at day 3 (1 male); and 1 dead at day 5 (1 female) 5000 mg/kg = 2 dead at 23 hours (1 male and 1 female); 5 dead at day 2 (4 males and 1 female); and 3 dead at day 3 (3 females)
Remarks:	A variety of abnormal signs occurred on the day of dosing. Several animals exhibited hypoactivity, red nasal discharge, urinary staining, partially closed eyes, prostration, and decreased food consumption. Signs seen in a few animals (in most groups) included ataxia, tremors, clear nasal and oral discharges, wet rales, soft stool, fecal staining and abdominal griping. A few animals exhibited blue pigmentation and hypothermia on the day of dosing; by day 2 or 3, a majority of the survivors were exhibiting these signs. Postmortem examinations of animals, which were found dead, revealed a variety of changes, primarily blue pigmentation of all/most soft tissues and/or blue fluid in the gastrointestinal tract and urinary bladder. Other changes seen in most animals, which were, found dead

	included changes in the stomach, intestine and urinary bladder which were suggestive of an irritant and/or corrosive effect
Conclusions	
Data Quality	
Reliability (Klimisch):	1B
Remarks:	Reliable without restrictions; comparable to guideline study.
Reference	Biodynamics Inc. 1987. Acute Oral Toxicity Study in Rats. Unpublished report 4086-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828
Other Available Reports	Chevron. 1991. The Acute Oral Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] in Male and Female Rats. Unpublished Report No. 90-18. 1A: Reliable without restrictions: guideline study. MHW, Japan. 1993. Single Oral Toxicity Test of 1,4-Diethylbenzene in Rats. Unpublished Report for OECD-SIDS program. 4B: Not assignable; only secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

ACUTE ORAL TOXICITY (B)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated

Method

Method/guideline followed:	FIFRA/TSCA guidelines
Type:	LD_{50}
GLP:	Yes
Year:	1990-1991
Species/Strain:	Sprague-Dawley rats
Sex:	male and female
No. of animals per sex per dose:	5
Vehicle:	Not stated
Route of administration:	Oral/gastric intubation
Remarks:	At start of the experiment, males were 74 days old with a weight of 225 to 340 grams, and females were 81 days old with a weight of 170 to 254 grams. Room temperature was 17 - 23°C, and relative humidity was between 45 – 65% during the study. Animals were observed for 14 days postdose.

Results

LD_{50} value:	= 6900 mg/kg for males; and 4700 mg/kg for females (95% confidence limits of 3800 to 12100 g/kg) Number of deaths: 3400 mg/kg = males and females: no deaths 4300 mg/kg = 1 dead on day 4 (males); 2 dead on day 3 (females) 5000 mg/kg = 1 dead on day 1 (males); 3 dead on days 2-3 (females) 7700 mg/kg = 3 dead on days 3-6 (males); 5 dead on days 2-4 (females)
Remarks:	Treated animals displayed similar patterns of toxicity that usually began with some variety of motor dysfunction (awkward gait, splayed fore- and hindlimbs) beginning approximately 6.5 hours after dosing. Tremors were also observed in some treated females of the 4300, 5000, and 7700 mg/kg dose groups, beginning 6 hours post-dosing. Cyanosis was observed in one treated male treated with 5000 mg/kg, 6.5 hours post-dosing. At Day 1, symptomology consistent with generalized central nervous system depression was observed in all treated animals. Several treated animals were found either comatose or unable to maintain normal posture. All treated animals exhibited reductions in spontaneous motor activity, abnormal righting reflexes, and decreases in responsiveness to extraneous sensory stimuli. Green urine was also observed on Day 1 in all dose groups.

Other signs of toxicity included but were not limited to reductions in the rate and depth of breathing, red nasal discharge, ocular and anogenital discharge, diarrhea, reduced pupil response, mydriasis, lacrimation, and partial palpebral closure. On Day 2, cyanosis developed within all treatment groups with the exception of females treated with 3400 and 4300 mg/kg. No treatment-related signs of toxicity were observed after Day 8 in surviving animals. At necropsy, dark fluid was found in the bladders of some animals treated with >3400 mg/kg. The gross appearance of these bladders were normal.

Conclusions

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restrictions; guideline study.

Reference

Chevron. 1991. The Acute Oral Toxicity of Polyethylbenzene [Mixed Diethylbenzenes] in Male and Female Rats. Unpublished Report No. 90-18.

Other Available Reports

Biodynamics Inc. 1987. Acute Oral Toxicity Study in Rats. Unpublished report BD-87-093. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828
1B: Reliable without restrictions; comparable to guideline study.

MHW, Japan. 1993. Single Oral Toxicity Test of 1,4-Diethylbenzene in Rats. Unpublished Report for OECD-SIDS program.
4B: Not assignable; only secondary literature.

Other

Last changed: September 4, 2001

Remarks:

ACUTE DERMAL TOXICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	FIFRA/TSCA guidelines
Type:	LD_{50}
GLP:	Yes
Year:	1987
Species/Strain:	New Zealand White rabbits
Sex:	male and female
No. of animals per sex per dose:	5
Vehicle:	Not stated
Route of administration:	Dermal
Remarks:	At start of the experiment, animals were at least 8 weeks old. The males weighed between 2.3-2.6 kg, and the females weighed between 2.6-2.7 kg. Room temperature was 60-70^{o}F, and relative humidity was between 30-70% during the study. Animals were observed for 14 days postdose.

Results

LD_{50} value:	= >5000 mg/kg
Remarks:	All animals exhibited body weight losses or no weight change at Day 7, but most gained weight between Days 7 and 14. Except for fissuring exhibited at a small portion of the dose site, in one animal, no severe dermal effects were seen. Decreased food consumption was exhibited by all ten animals on the day after dosing; by four animals on Day 4; and by one animal on Day 10.

Conclusions

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions; guideline study.

Reference

Biodynamics Inc. 1987. Acute Dermal Toxicity Study in Rabbits. Unpublished report 4087-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828

Other Available Reports

Chevron, 1991. The acute dermal toxicity of polyethylbenzene [Mixed Diethylbenzenes] (MF-335) in rats. Unpublished Report. Study Number CEHC 3172, Chevron Environmental Health Center, Richmond, CA.

Other

Last changed:	September 13, 2001
Remarks:	

ACUTE DERMAL TOXICITY (B)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	FIFRA/TSCA guidelines
Type:	LD_{50}
GLP:	Yes
Year:	1990
Species/Strain:	Sprague-Dawley rats
Sex:	male and female
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Dermal
Remarks:	At start of the experiment, males were 71 weeks old and the females were 77 weeks old. The males weighed between 346 and 380 grams, and the females weighed between 228 and 266 grams. Room temperature was 20-22^{o}C, and relative humidity was between 34-56% during the study. Animals were observed for 14 days postdose.

Results

LD_{50} value:	= >2000 mg/kg
Remarks:	Compound-related signs of toxicity were limited to a yellow anogenital discharge in a single treated male. Skin irritation consisting of red, swollen and scabbed skin was more persistent and severe in treated animals than in controls. A significant decrease in mean body weight gain was observed in treated males on Days 0-2.

Conclusions

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restrictions; guideline study.

Reference

Chevron, 1991. The acute dermal toxicity of polyethylbenzene [Mixed Diethylbenzenes] (MF-335) in rats. Unpublished Report. Study Number CEHC 3172, Chevron Environmental Health Center, Richmond, CA.

Other Available Reports

Biodynamics Inc. 1987. Acute Dermal Toxicity Study in Rabbits. Unpublished report 4087-87. Submitted to EPA by Monsanto Inc., as EPA Doc. No. 8EHQ-0892-8828

Other

Last changed:	September 13, 2001
Remarks:	

REPEATED DOSE TOXICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
Test type:	Inhalation
GLP:	Yes
Year:	1991-1992
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Inhalation
Duration of test:	3 months
Doses/concentration levels:	200, 600, and 1200 mg/m^3
Sex:	Male and female
Exposure period:	10 weeks (mixture) and 8 weeks (isomers)
Frequency of treatment:	6 hours/day, five days/week
Control group and treatment:	Concurrent
Postexposure observation period:	None
Statistical methods:	Dunnett's Multiple Comparison Test (two-tailed) for inlife body weights. Hematology data, clinical chemistry data, terminal body weights, absolute organ weights and organ/body weight ratios were evaluated by decision-tree statistical analyses which, depending on the results of tests for normality and homogeneity of variances (Bartlett's Test), utilized either parametric (Dunnett's Test and Linear Regression) or non-parametric (Kruskal-Wallis, Jonckheere's and/or Mann-Whitney Tests) routines to detect differences and analyze for trends. Fisher's Exact Test (one-tailed) was used for incidence of microscopic lesions
Remarks:	There were 10 rats/group. The mean analytical concentrations were 0, 190, 610, and 1400 mg/m^3. Each exposure level was sampled four times daily, and the control chamber was sampled weekly, for test material concentration. Animals were checked twice daily for mortality and following each exposure for gross signs of toxicity. During exposure, visible animals were observed for signs of toxicity. Body weights and clinical observations were performed weekly. Ophthalmic examinations were performed pretest on all animals and just prior to termination on control and high-exposure level animals. Clinicopathologic examinations were performed at termination. All animals were given a gross necropsy. All retained tissues from the control and high-exposure level groups were examined microscopically.

Results

NOAEL:	190 mg/m^3
Toxic response/effects:	Decreased mean body weights in the high-dose group animals throughout the study. There were no abnormal clinical observations, which were considered to be treatment-related. There were no ocular abnormalities attributed to administration of the test material. Treatment-related changes in hematologic parameters included moderate decreases in total white cell and lymphocyte counts in the mid- and high-exposure level males. Abnormal sera color (blue or blue-gray) was observed in high-exposure level animals of both sexes. Treatment-related changes in serum chemistry parameters included decreases in ALT, AST, and CPK in high-exposure level females and increases in potassium in high-level males and phosphorus in males from the high-exposure group and females from the mid- and high-exposure groups. An abnormal blue-gray color was observed in most tissues from all but one high-exposure animal. At the mid-exposure level, the same color was observed in brains of eight males and all females and in the urinary bladders of five females and one male. This abnormal color probably resulted from the presence of the parent chemical or a metabolite in these tissues. However, there were no other gross or microscopic changes attributed to the test material.
Statistical results:	
Remarks:	

Conclusions

Repeated exposures to Mixed Diethylbenzenes (CAS No. 25340-17-4) did not result in any target organ toxicity. This endpoint has been adequately covered.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; EPA Guideline study.

Reference

Kaempfe, T. A. and Thake, D. C. 1993. Three-Month Inhalation Study of MCS 2313 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

Other Available Reports

Gagnaire, F., Marignac, B., and de Ceaurriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2): 105-112.
3D: Not reliable. Relevant methodological deficiencies.

Gagniare, F., Ensminger A., Marignac, B., and De Ceaurriz (1991) Possible involvement of 1,2-diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and DeCeaurriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked potential in rats. J. Applied Toxicology 12(5): 335-342.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceaurriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350.
3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.
4A: Not assignable; only short abstract available.

Other

Last changed: September 4, 2001
Remark:

REPEATED DOSE TOXICITY (B)

Test Substance

Identity:	Diethylbenzene (DEB) mixture (approx. 7% 1,2-diethylbenzene, 58% 1,3-diethylbenzene 35% 1,4-diethylbenzene) or individual diethylbenzene isomers
Purity:	95% 1,2-diethylbenzene, 99% 1,3-diethylbenzene, 96% 1,4-diethylbenzene
Remarks:	

Method

Method/guideline followed:	Not stated
Test type:	Oral
GLP:	No
Year:	
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Oral gavage
Duration of test:	8 or 10 weeks
Doses/concentration levels:	500 or 750 mg/kg (in olive oil) for DEB mixture; 100 mg/kg for 1,2-diethylbenzene; and 500 mg/kg for 1,3- and 1,4-diethybenzene
Sex:	No specified
Exposure period:	10 weeks (mixture) and 8 weeks (isomers)
Frequency of treatment:	5 days/week (mixture and 1,3- and 1,4-diethylbenzene isomers); 4 days/week (1,2-diethylbenzene)
Control group and treatment:	Concurrent, given olive oil vehicle
Postexposure observation period:	8 weeks (isomer study only)
Statistical methods:	Differences in mean body weight, motor and sensory conduction velocities, and amplitude of the sensory action potential between experimental and control groups were analyzed using Student's t-test for independent data. Mean electrophysiological deficits in the tail nerve were also analyzed, as a function of the length of treatment, by least-squares regression.
Remarks:	There were 12 rats/group. Rats were subjected to neurophysiological measurements every week during the treatment period. The survivors were kept for observation and neurophysiological measurements during the post-exposure period. The motor conduction velocity (MCV) and sensory conduction velocity (SCV) of the tail nerve and the amplitude of the sensory action potential (ASAP) were adopted as parameters for testing peripheral nerve function in rats.

Results

LOAEL:	500 mg/kg (DEB mixture); and 100 mg/kg (1,2-diethylbenzene)
NOAEL:	500 mg/kg (1,3- and 1,4-diethylbenzene)
Toxic response/effects:	Described below

Statistical results:	Described below
Remarks:	Diethylbenzene mixture Rats given diethylbenzene (DEB) mixture with either 500 or 750 mg/kg exhibited a blue discoloration of the skin and urine as soon as the 3rd day of treatment. A significant reduction in weight gain was observed from the first week of treatment in the group treated with 750 mg/kg. Two animals died in the 750 mg/kg dose group during the first week of treatment. Two rats died in the 500 mg/kg group during the 4th and 7th weeks of treatment. No animals died in the control group. Rats in the DEB-dosed groups developed severe weakness in hind limbs and disturbances in gait from the 4th week of treatment. This weakness got worse in the following weeks, resulting in a complete paralysis of the hind limbs for some rats. There was a time-dependent decrease in MCV, SCV, and ASAP. Diethylbenzene isomers Rats given 1,2-diethylbenzene developed the same symptoms (decreased body weight, blue discoloration of skin and urine, weakness of hind limbs, paralysis) as those described for the diethylbenzene mixture. One rat died in the first week of treatment and another died in the 5th week of treatment. 1,3- and 1,4-Diethylbenzene-treated rats did not display any signs of neurotoxicity or any other signs of systemic toxicity. During the recovery period, the 1,2-diethylbenzene treated rats regained weight, became more mobile but presented trailing hind limbs, when attempting to walk. On the 4th week of recovery, all animals treated with 1,2-diethylbenzene succeeded in standing up. A time-dependent decrease in MCV, SCV, and ASAP was observed in animals dosed with 1,2-diethylbenzene, but not with 1,3- or 1,4-diethylbenzene.
Conclusions	Oral exposure to diethylbenzene mixture and 1,2-diethylbenzene produced adverse effects on the peripheral nervous system, whereas 1,3- and 1,4-diethylbenzene did not.
Data Quality	
Reliability (Klimisch):	3D
Remarks:	Not reliable. Relevant methodological deficiencies.
Reference	Gagnaire, F., Marignac, B., and de Ceaurriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2): 105-112.
Other Available Reports	Gagniare, F., Ensminger A., Marignac, B., and De Ceaurriz (1991) Possible involvement of 1,2-

diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and DeCeaurriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked potential in rats. J. Applied Toxicology 12(5): 335-342.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceaurriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350.
3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.
4A: Not assignable; only short abstract available.

Other

Last changed: September 13, 2001
Remark:

REPEATED DOSE TOXICITY (C)

Test Substance

Identity:	Diethylbenzene (DEB) mixture (approx. 6% 1,2-diethylbenzene, 66% 1,3-diethylbenzene 28% 1,4-diethylbenzene)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Test type:	Inhalation
GLP:	No
Year:	
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Inhalation
Duration of test:	18 weeks
Doses/concentration levels:	500, 700, and 900 ppm in experiment A; 600 and 800 ppm in experiment B
Exposure period:	18 weeks
Frequency of treatment:	6 hours/day, 5 days/week
Control group and treatment:	Concurrent
Postexposure observation period:	6 or 7 weeks
Statistical methods:	Statistical differences among groups were evaluated for each variable on each session by one-way analysis of variance. *Post hoc* individual mean comparisons were made with Duncan's multiple range tests.
Remarks:	There were 12 rats/group in experiment A and 15 rats/group in experiment B. Rats were subjected to neurophysiological measurements every two weeks during the entire exposure period in experiment A, and every two weeks for the first 9 weeks of exposure in experiment B and then every three weeks thereafter. The survivors were kept for observation and neurophysiological measurements during the post-exposure period. The motor conduction velocity (MCV) and sensory conduction velocity (SCV) of the tail nerve and the amplitude of the sensory action potential (ASAP) were adopted as parameters for testing peripheral nerve function in rats in experiment A. In experiment B, only brainstem auditory evoked potential (BAEP) was measured.

Results

LOAEL:	500 ppm
Toxic response/effects:	Described below
Statistical results:	Described below
Remarks:	Experiment A

Exposure to DEB reduced weight gain from the first week of exposure in each group. There was no mortality in the control, 500 or 700 ppm exposed groups. In the 900 ppm group, one animal was euthanized on the fifth week of exposure due to an abscess at the neck. The animals of the 700 and 900 ppm exposed groups were prostrate during the exposure period but recovered a few hours after the end of the exposure period. Rats in the all DEB-exposed groups developed blue skin discoloration after three weeks of exposure. No animal in any group exhibited disturbances in gait or other signs of neurotoxicity. There was a time- and concentration-dependent decrease in MCV, SCV, and ASAP, which did not completely reversed during the 6-week recovery period.

Experiment B

Weight gain was reduced in the DEB-exposed groups. From the third week of exposure, the DEB-exposed groups exhibited the blue skin discoloration. At the end of the exposure period, some animals exhibited disturbances in gait and one animal in the 800 ppm group had partial paralysis in the hindlimbs. Two animals died in the 800 ppm group during the exposure period, and 8 animals/group had to be euthanized during the study because they lost their head plugs during the recording sessions. There was a time- and concentration dependent increase in both the peak latencies of all BAEP components and the interpeak (I-V) differences. Partial, but not complete reversal, occurred during the 7-week recovery period.

Conclusions

Inhalation exposure to diethylbenzene mixtures appear to have adverse effects on the peripheral and central nervous system. There seems to be, however, some inconsistencies between the two experiments with regards to the clinical signs of peripheral nervous system damage. The authors proposed that this difference may be due to the age of the rats used in these two experiments, 9-and 19-week old, respectively.

Data Quality

Reliability (Klimisch): 3D

Remarks: Not reliable. Relevant methodological deficiencies.

Reference

Gagnaire, F., Becker, M. N., Marignac, B., Bonnet, P., and De Ceaurriz, J. (1992) Diethylbenzene inhalation-induced electrophysiological deficits in peripheral nerves and changes in brainstem auditory evoked

potentials in rats. J. Applied Toxicology 12(5): 335-342.

Other Available Reports

Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 2313 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.

Gagnaire, F., Marignac, B., and de Ceaurriz, J. (1990) Diethylbenzene-induced sensorimotor neuropathy in rats. J. Applied Toxicology 10(2) 105-112.
3D: Not reliable. Relevant methodological deficiencies.

Gagniare, F., Ensminger A., Marignac, B., and De Ceaurriz (1991) Possible involvement of 1,2-diacetylbenzene in diethylbenzene-induced neuropathy in rats. J. Appl. Toxicology 11(4) 261-268.
3D: Not reliable. Relevant methodological deficiencies.

Gagnaire, F., Becker, M. N., and De Ceaurriz, J. (1992) Alteration of brainstem auditory evoked potentials in diethylbenzene and diacetylbenzene-treated rats. J. Applied Toxicology 12(5): 343-350.
3D: Not reliable. Relevant methodological deficiencies.

MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.
4A: Not assignable; only short abstract available.

Other

Last changed: September 4, 2001
Remarks:

GENETIC TOXICITY *IN VITRO* (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	
Remarks:	

Method

Method/guideline followed:	OECD Method No. 471
Type:	*Salmonella* reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1990
Species/Strain:	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 with S-9 activation and without S-9 activation
Metabolic activation:	Liver S-9 fraction from Aroclor 1254 pretreated (injected, ip) male Sprague-Dawley rats.
Concentrations tested:	0.003, 0.01, 0.033, 0.1, 0.333, 1.0, 3.33, 10.0 mg/plate
Statistical methods:	Not stated
Remarks:	Positive (2-aminoanthracene, 2-nitrofluorene, and sodium azide) and negative controls were included. Eight doses in addition to the concurrent solvent and positive controls were tested on each strain in the presence of S-9 mix or buffer. Three plates were used, and the results were confirmed in an independent experiment.

Results

Result:	Negative
Cytotoxic concentration:	$\geq$ 1 mg/plate
Genotoxic effects:	Negative
Statistical results:	Statistically significant increases in the number of revertants were observed for TA98 and TA100 in the presence of metabolic activation. These responses were not reproducible and were, therefore, not considered to be biologically significant.
Remarks:	

Conclusions Mixed diethylbenzenes (25340-17-4) did not cause mutations to *S.* typhimurium in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; OECD guideline study.

Reference

Chevron. 1991. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.

Other Available Reports

Stankowski, L. F. 1988 Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company.
1A: Reliable without restriction; EPA guideline study.

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 2313 (mixed diethylbenzene stream, CAS No. 25340-17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.
1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.
4B: Not assignable; only secondary literature.

Other

Last changed:	September 4, 2001
Remarks:	

GENETIC TOXICITY *IN VITRO* (B)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not specified
Remarks:	

Method

Method/guideline followed:	OECD Method No. 471
Type:	*E. coli*
System of testing:	Bacterial
GLP:	Yes
Year:	1990
Species/Strain:	*E.* coli WP2 uvrA with S-9 activation and without S-9 activation
Metabolic activation:	Liver S-9 fraction from Aroclor 1254 pretreated (injected, ip) male Sprague-Dawley rats.
Concentrations tested:	0.003, 0.01, 0.033, 0.1, 0.33, 1.0, 3.33, 10.0 mg/plate
Statistical methods:	Not stated.
Remarks:	Positive (2-aminoanthracene and ICR-191) and negative controls were included. Eight doses in addition to the concurrent solvent and positive controls were tested in the presence of S-9 mix or buffer. Three plates were used, and results were confirmed in an independent experiment.

Results

Result:	Negative
Cytotoxic concentration:	$\geq$ 1 mg/plate
Genotoxic effects:	Negative
Statistical results:	
Remarks:	Cytotoxicity was also observed in WP2 uvrA without S-9 at dose levels of 0.1 and 0.33 mg/plate in a single experiment. Since WP2 uvrA is generally more resistant to toxicity than the *Salmonella* strains (which tested in the same experiment; see 5.5A), and the toxicity was observed also in the positive controls where it was not expected, it was concluded that the cytotoxic response in WP2 uvrA without activation at 0.1 and 0.33 mg/plate was probably not treatment-related.

Conclusions Mixed diethylbenzenes (25340-17-4) did not cause mutations to *E.* coli in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; OECD guideline study.

Reference	Chevron. 1991. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.
Other Available Reports	Stankowski, L. F. 1988 Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company. 1A: Reliable without restriction; EPA guideline study. Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 2313 (mixed diethylbenzene stream, CAS No. 25340-17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002. 1A: Reliable without restriction; EPA guideline study. MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program. 4B: Not assignable; only secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

GENETIC TOXICITY *IN VITRO* (C)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
Type:	*Salmonella* reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1988
Species/Strain:	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 with S-9 activation and without S-9 activation
Metabolic activation:	Liver S-9 fraction from Aroclor 1254 pretreated male Sprague-Dawley rats.
Concentrations tested:	0.00167, 0.005, 0.0167, 0.05, 0.167, 0.5 mg/plate
Statistical methods:	Not stated
Remarks:	Positive (2-aminoacridine, 2-nitrofluorene, 2-antramine and sodium azide) and negative controls were included. Six doses in addition to the concurrent solvent and positive controls were tested on each strain in the presence of S-9 mix or buffer. Three plates were used, and the results were confirmed in an independent experiment.

Results

Result:	Negative
Cytotoxic concentration:	$\geq$ 0.05 mg/plate
Genotoxic effects:	Negative
Statistical results:	
Remarks:	

Conclusions Mixed diethylbenzenes (25340-17-4) did not cause mutations to *S.* typhimurium in this *in vitro* genetic toxicity test. The bacterial mutation potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study.

Reference

Stankowski, L. F. 1988 Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company.

Other Available Reports

Chevron. 1991. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.
1A: Reliable without restriction; OECD guideline study.

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 2313 (mixed diethylbenzene stream, CAS No. 25340-17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.
1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.
4B: Not assignable; only secondary literature.

Other

Last changed:	September 4, 2001
Remarks:	

GENETIC TOXICITY *IN VITRO* (D)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
Type:	Chromosomal aberration assay
System of testing:	mammalian cells
GLP:	Yes
Year:	1988
Species/Strain:	Chinese Hamster Ovary cells with and without S-9 activation
Metabolic activation:	Liver S-9 fraction from Aroclor 1254 pretreated Sprague-Dawley rats.
Concentrations tested:	25, 40, 50, 60, and 75 ug/ml
Statistical methods:	Chi-square analysis was used to analyze the number of cells with structural aberrations. Dunnett's t-test was used to analyze structural aberrations per cell.
Remarks:	Positive (methyl methane sulfonate and cyclophosphamide) and negative controls were included. Five doses in addition to the concurrent solvent and positive controls were tested in the presence of S-9 mix or buffer. Duplicate samples per treatment condition were used and the cells were harvested at 12 an 24 hours after initiation of treatment.

Results

Cytotoxic concentration:	$\geq$ 50 ug/ml
Genotoxic effects:	Negative
Statistical results:	
Remarks:	

Conclusions Mixed diethylbenzenes (25340-17-4) did not cause any statistically significant increase in the number of cells with structural aberrations or in the average structural aberrations per cell. The clastogenic potential of mixed diethylbenzenes (25340-17-4) has been adequately characterized by this study.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; EPA guideline study.

Reference

Myers, C.A., and Fahey, P.M. (1989) In Vitro Cytogenetics Study on MCS 2313 (mixed diethylbenzene stream, CAS No. 25340-17-4). Conducted at Monsanto Company Environmental Health Laboratory, Report No. MSL-9002.

Other Available Reports

Chevron. 1991. Microbial/Microsome Reverse Mutation Plate Incorporation Assay with Polyethylbenzene [Mixed Diethylbenzenes] (MF-355). Unpublished Report No. 90-23.
1A: Reliable without restriction; OECD guideline study.

Stankowski, L. F. 1988 Ames/*Salmonella* Plate Incorporation Assay. Pharmakon Research International, Inc. Study No. 301-MO-002-88. Conducted for Monsanto Company.
1A: Reliable without restriction; EPA guideline study.

MWH, Japan. 1993. Reverse Mutation Test of 1,4-Diethylbenzene on Bacteria. Unpublished Report for OECD-SIDS program.
4B: Not assignable; only secondary literature.

Other

Last changed:	September 4, 2001
Remarks:	

GENETIC TOXICITY *IN VIVO*

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not specified
Remarks:	

Method

Method/guideline followed:	OECD Method No. 474
Type:	Micronuclei formation in bone marrow erythrocytes
GLP:	Yes
Year:	1990
Species:	Mouse
Strain:	CD-1
Sex:	Male and female
Route of administration:	Intraperitoneal
Doses/concentration levels:	1000, 2000, and 4000 mg/kg (diluted with peanut oil)
Exposure period:	Single dose
Statistical methods:	
Remarks:	Vehicle and positive controls were dosed intraperitoneally with peanut oil and cyclophosphamide, respectively. Number of animals: 18/sex/group, except for the positive control group (5/sex). Bone marrow smears, 5 animals/sex/dose, were made at approximately 24, 48, and 72 hours post-dosing, according to the method of Schmid (1976)[1]. The slides were fixed in methanol and stained with 5% Giemsa for approximately 20 minutes. The percentage of PCE was calculated by counting a total of >200 erythrocytes. On each slide, a total of 1000 PCEs were evaluated for the presence of micronuclei.

[1]Schmid, W (1976). The micronucleus test for cytogenetic analysis. In: A. Hollaender (Ed), Chemical Mutagens, vol. 4, pp. 31-53, Plenum, NY

Results

Cytotoxicity:	Cytotoxicity was noted in females dosed with 4000 mg/kg and sampled at 48 hours.
Genotoxic effects:	No treatment-related effect on increased micronucleated polychromatic erythroctyes in either sex.
NOEC or LOAEC:	1000 mg/kg
Statistical results:	No statistically significant differences between mixed diethylbenzene-exposed animals and controls.
Remarks:	Evidence of toxicity was found at $\geq$ 2000 mg/kg in both sexes. Clinical signs of toxicity observed were decreased motor activity, collapse, labored breathing, convulsions, and weakness. In addition, on Day 1, one male at 2000 mg/kg and three males and one female at 4000 mg/kg

	died before the scheduled sampling time; two moribund females at 4000 mg/kg were euthanized.
Conclusions	Under the conditions of this study, mixed diethylbenzene (25340-17-4) was considered non-genotoxic, since micronuclei were not induced in the bone marrow erythrocytes of mice.
Data Quality	
Reliability (Klimisch):	1A
Remarks:	Reliability without restriction; OECD guideline study.
References	Chevron. 1991. Micronucleus Assay in Mouse Bone Marrow Erythrocytes: Polyethylbenzene [Mixed Diethylbenzenes]. Unpublished Report No. 90-24.
Other Available Reports	MHW, Japan. 1993. In Vitro Chromosomal Aberration Test of 1,4-Diethylbenzene on Cultured Chinese Hamster Cells. Unpublished Report for the OECD-SIDS program. 4B: Not assignable; only secondary literature.
Other	
Last changed:	September 4, 2001
Remarks:	

REPRODUCTIVE TOXICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
Test type:	Inhalation
GLP:	Yes
Year:	1991-1992
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Inhalation
Duration of test:	3 months
Doses/concentration levels:	200, 600, and 1200 mg/m^3
Exposure System:	Low exposure level test atmospheres were generated using a Laskin-style nebulizer/spraybar positioned in the supply air chamber inlet. Test material was delivered using syringe pump. The mid- and high-exposure level test atmospheres were generated using a spray nozzle directed down from the top of the chamber. Test material was delivered for the mid- and high-level chambers with a valveless pump. The concentration of test material in the chambers was controlled by regulating the flowrate of the material from the pumps.
Sex:	Male and female
Exposure period:	10 weeks (mixture) and 8 weeks (isomers)
Frequency of treatment:	6 hours/day, five days/week
Control group and treatment:	Concurrent
Postexposure observation period:	None
Statistical methods:	Dunnett's Multiple Comparison Test (two-tailed) for in-life body weights. Absolute organ weights and organ/body weight ratios were evaluated by decision-tree statistical analyses which, depending on the results of tests for normality and homogeneity of variances (Bartlett's Test), utilized either parametric (Dunnett;s Test and Linear Regression) or non-parametric (Kruskal-Wallis, Jonckheere's and/or Mann-Whitney Tests) routines to detect differences and analyze for trends. Fisher's Exact Test (one-tailed) was used for incidence of microscopic lesions
Remarks:	There were 10 rats/group. The mean analytical concentrations were 0, 190, 610, and 1400 mg/m^3. Each exposure level was sampled four times daily, and the control chamber was sampled weekly, for test material concentration. Animals were checked twice daily for mortality and following each exposure for gross signs of toxicity. During exposure, visible

	animals were observed for signs of toxicity. Body weights and clinical observations were performed weekly. All animals were given a gross necropsy. All retained tissues, including ovaries, pituitary, prostate, seminal vesicles, testes with epididymides, and uterus (corpus and cervix), from the control and high-exposure level groups were examined microscopically.
Results	
NOAEL:	190 mg/m^3
Toxic response/effects:	Decreased mean body weights in the high-dose group animals throughout the study. There were no abnormal clinical observations which were considered to be treatment-related. An abnormal blue-gray color was observed in most tissues from all but one high-exposure animal. At the mid-exposure level, the same color was observed in brains of eight males and all females and in the urinary bladders of five females and one male. This abnormal color probably resulted from the presence of the parent chemical or a metabolite in these tissues. However, there were no other gross or microscopic changes in the reproductive tissues attributed to the test material.
Statistical results:	
Remarks:	
Conclusions	Mixed Diethylbenzene Stream (25340-17-4) does not appear to target the reproductive organs in rats.
Data Quality	
Reliability (Klimisch):	2C
Remarks:	Reliable with restrictions; comparable to guideline study with acceptable restrictions.
Reference	Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 2313 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570.
Other Available Reports	MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program. 4A: Not assignable; only short abstract available.
Other	
Last changed:	September 4, 2001
Remark:	

REPRODUCTIVE TOXICITY (B)

Test Substance

Identity:	1,4-Diethylbenzene (CAS No. 105-05-5)
Purity:	97.2%
Remarks:	

Method

Method/guideline followed:	OECD Guideline No. 422
Test type:	Oral gavage
GLP:	Yes
Year:	1993
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Oral gavage
Duration of test:	Male: 44 days including 14 days before mating Female: 14 days before mating to lactation day 3
Doses/concentration levels:	30, 150, and 750 mg/kg
Sex:	Male and female
Exposure period:	Male: 44 days including 14 days before mating Female: 14 days before mating to lactation day 3
Frequency of treatment:	7 days/week
Control group and treatment:	Concurrent
Postexposure observation period:	None
Statistical methods:	Not stated
Remarks:	There were 12 rats/sex/group.

Results

NOAEL:	350 mg/kg/day?
Toxic response/effects:	Male and female copulation and fertility indices, pregnancy rates, and implantation sites were comparable among groups. The number of live and dead pups, the number of litters with live offspring, the mean litter size, and the male-to-female ratio were comparable among the groups on lactation day 0. There were no differences in mean pup weights across groups. No differences were found in external observations; and no remarkable findings were observed at necropsy in pups found dead prior to lactation day 4. Duration of gestation was slightly, but statistically significantly, increased in the 750 mg/kg group and there was a statistically significant decrease in pup survival on day 4 in the 750 mg/kg group; however, the investigators did not consider these findings treatment-related.
Statistical results:	
Remarks:	

Conclusions	1,4-Diethylbenzene (105-05-5) does not appear to be a reproductive toxicant, although a slight effect was observed on duration of gestation.
Data Quality	
Reliability (Klimisch):	4A
Remarks:	Not assignable; only short abstract available.
Reference	OECD-SIDS Dossier on 1,4-Diethylbenzene (CAS No. 105-05-5). MHW, Japan (1993) Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for OECD-SIDS program.
Other Available Reports	Kaempfe, T. A. and Thake, D. C. Three-Month Inhalation Study of MCS 2313 [Mixed Diethylbenzenes] in Sprague-Dawley Rats. Monsanto Environmental Health Laboratory Report No. MSL-12570. 2C: Reliable with restrictions; comparable to guideline study with acceptable restrictions.
Other	
Last changed:	September 4, 2001
Remark:	

DEVELOPMENTAL TOXICITY/TERATOGENICITY (A)

Test Substance

Identity:	Mixed Diethylbenzene Stream (CAS No. 25340-17-4)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	EPA Guidelines
GLP:	Yes
Year:	1992
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Oral gavage
Doses/concentration levels:	20, 100, 200 mg/kg/day (in corn oil)
Sex:	Female
Exposure period:	Day 6 through 15 of gestation
Frequency of treatment:	7 days/week
Control group and treatment:	Concurrent, received 5 ml/kg corn oil
Duration of test:	Day 20 of gestation
Statistical methods:	Continuous maternal and fetal data, including body weights, body weight gain, food consumption, number of fetuses, implantation sites and corpora lutea, were analyzed using one-way analysis of variance (ANOVA) followed by Dunnett's test. The Mann-Whitney U test was used to compare post-implantation loss and resorptions. Fetal sex ratios were analyzed using the Chi-Square test. Fisher's Exact test was used to analyze the incidence and number of fetal malformations and variations utilizing the dam (litter) as the experimental unit.
Remarks:	Twenty-five female rats were assigned to each group. The animals were observed daily for clinical signs of toxicity. Body weights and food consumption were measured on gestation day 0, 6, 9, 12, 16, and 20. Surviving females were euthanized on gestation day 20 and subjected to cesarean section. Fetuses were individually weighed, sexed and examined for external, visceral and skeletal abnormalities.

Results

Maternal toxicity NOAEL:	= 20 mg/kg/day
Developmental toxicity NOAEL:	= 100 mg/kg/day
Actual dose received:	0, 20, 100, or 200 mg/kg/day
Maternal data:	There were no treatment-related mortality or clinical signs of toxicity. Mean maternal body weight gain and food consumption statistically reduced at the 100 and 200 mg/kg/day groups throughout the study. Greenish-blue discoloration of the amniotic sac was observed in a dose-related manner at the 100 and 200 mg/kg/day levels.

Fetal data:	Mean fetal body weight was statistically reduced at the 200 mg/kg/day level when compared to the control group. All other cesarean parameters were comparable among groups. No treatment-related malformations or developmental variations were observed.
Statistical results:	
Remarks:	

Conclusions

Oral gavage dosing with up to 200 mg/kg/day of mixed diethylbenzene (25340-17-4) did not produce a teratogenic response in rats. Maternal toxicity occurred at dosages that were lower than that which produced developmental toxicity.

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliability without restriction; EPA guideline study.

Reference

Mercieca, M. D. 1992 Teratology Study in Rats with MCS 2313 [mixed diethylbenzene]. Springborn Laboratories, Inc. Report No. 30344.228. Conducted for Monsanto Company.

Other Available Reports

Saillenfait, A. M.., Payan, J. P., Langonné. I., Gallissot, F., Sabaté, J. P., Beydon, D., and Fabry, J. P. (1999) Assessment of the developmental toxicity and placental transfer of 1,2-diethylbenzene in rats. Food Chemical Toxicol. 37: 1089-1096.
2B: Reliable with restrictions; basic data given, comparable to guidelines/standards.

MHW, Japan. 1993. Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for the OECD-SIDS program.
4A: Not assignable; only short abstract available.

Other

Last changed:	September 4, 2001
Remarks:	

DEVELOPMENTAL TOXICITY/TERATOGENICITY (B)

Test Substance

Identity:	1,2-Diethylbenzene
Purity:	>99%
Remarks:	

Method

Method/guideline followed:	Not stated
GLP:	Not stated
Year:	
Species:	Rat
Strain:	Sprague-Dawley
Route of administration:	Oral gavage
Doses/concentration levels:	5, 15, 25, or 35 mg/kg/day
Sex:	Female
Exposure period:	Day 6 through 20 of gestation
Frequency of treatment:	7 days/week
Control group and treatment:	Concurrent, received 2 ml/kg corn oil
Duration of test:	Day 21 of gestation
Statistical methods:	Number of implantation sites and live fetuses, food consumption and various body weights were analyzed by one-way analysis of variance, followed by Dunnett's test if differences were found. The frequencies of non-surviving implants, resorptions, males, and anomalies among litters were evaluated by using Dixon-Massey test. Rates of pregnancy and incidence of litters with alterations were analyzed by using Fisher's test. Where applicable, least-squares analysis was carried out.
Remarks:	There were 28-29 female rats assigned to each group. All females were observed daily for clinical signs of toxicity. Food consumption was measured at 3-day intervals starting at gestation day (GD) 6. Maternal body weights were recorded on GD0, 6, 9, 12, 15, 18, and 21. On GD 21, the females were euthanized and the uteri were removed and weighed. Uterine contents were examined to determine the number of implantation sites, resorptions, and dead/live fetuses. Live fetuses were weighed, sexed, and examined for external anomalies. Half of the live fetuses for each litter were examined for internal soft tissue changes and the other half were processes for skeletal staining.

Results

Maternal toxicity NOAEL:	= 5 mg/kg/day
Developmental toxicity NOAEL:	= 5 mg/kg/day
Actual dose received:	5, 15, 25, and 35 mg/kg/day
Maternal data:	No animals died during the study. Maternal weight gain was significantly reduced during GD 6-9 in the $\geq$ 15 mg/kg dose groups, and for GD 18-21 in the 35 mg/kg dose group. Females dose with $\geq$ 15 mg/kg had

	significant dose-related decreases in maternal weight gain for GD 6-21 and in corrected weight gain. Maternal food consumption was significantly depressed during the initial and final three days of treatment at ≥ 15 mg/kg. Depression in food consumption persisted during GD 9-12 in the 25 mg/kg dose group, and during GD 9-12 and GD 15-18 in the 35 mg/kg dose group. Overall, food consumption on GD 6-21 was significantly decreased in the 25 and 35 mg/kg dose groups. There were no significant effects on the average number of implantations and live fetuses, on the incidence of non-surviving implants per litter, or on the fetal sex ratio.
Fetal data:	Fetal body weights in the ≥ 15 mg/kg dose groups were significantly reduced, and were dose-related. There was no evidence of a treatment-related effect in any malformations or variations.
Statistical results:	
Remarks:	
Conclusions	Oral gavage dosing with up to 35 mg/kg/day 1,2-diethylbenzene produced reduced fetal body weights, but no teratogenic effects . Developmental toxicity occurred only at dosages that produced maternal toxicity.
Data Quality	
Reliability (Klimisch):	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.
Reference	Saillenfait, A. M.., Payan, J. P., Langonné. I., Gallissot, F., Sabaté, J. P., Beydon, D., and Fabry, J. P. (1999) Assessment of the developmental toxicity and placental transfer of 1,2-diethylbenzene in rats. Food Chemical Toxicol. 37: 1089-1096.
Other Available Reports	Mercieca, M. D. 1992 Teratology Study in Rats with MCS 2313 [mixed diethylbenzene]. Springborn Laboratories, Inc. Report No. 30344.228. Conducted for Monsanto Company. MHW, Japan. 1993. Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test of 1,4-Diethylbenzene. Unpublished Report for the OECD-SIDS program. 4A: Not assignable; only short abstract available.
Other	
Last changed:	September 4, 2001
Remarks:	